REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. The claim amendments are supported by page 17, lines 20-21 of the specification. The amendment of Claim 19 is to describe that a dimer of single chain Fv is formed by culturing host animal cells producing the single chain Fv in serum-free medium and the formed dimer exists stably.

Priority

Certified copies of the foreign priority documents, which were transmitted by the International Bureau, are available on PAIR, therefore the examiner is respectfully requested to acknowledge receipt of these documents. Applicants are concurrently filing English translations of three priority applications.

IDS

Applicants submitted an IDS on April 25, 2006, citing 74 references. Acknowledgment of this IDS by return of the initialed SB 08 is respectfully requested by the applicant.

Specification

The specification has been amended to include a brief description of the drawings.

Claim Rejections Under 35 USC § 112, Indefiniteness

Applicants have amended the claims in order to overcome the rejections for indefiniteness. A single chain Fv (scFv) is secreted from host cells in serum-free medium and a dimer of scFv is formed in the medium. Single chain Fv dimer is automatically produced in serum-free medium and no specific process is needed except for using serum-free medium.

With respect to the rejection of claim 19 the amended claims recite that a dimer is formed by the use of serum-free medium and the formed dimer exists stably.

Claim Rejections Under 35 USC § 112, Enablement

Claims 18 and 19 have been amended to specify that the length of linker into 2-12 amino acids. A person skilled in the art, who has read the specification, especially Examples 5 and 6, can easily practice the present invention without undue experimentation because the length of linker is recited as being 2-12 amino acids and a dimer of scFv having such a linker is readily produced in serum-free medium.

Claim Rejections Under 35 USC § 102

Fukushima (U.S. 20040073013) is derived from PCT/JP01/01912, to which this application claims priority. Therefore Fukushima cannot be prior art. Applicants also attach hereto English translations of the three Japanese-language priority applications.

Claim Rejections Under 35 USC § 103

The present invention is not obvious from Kortt, Dorai (as evidenced by Verma) and Keen as explained in the following.

Kortt discloses the production of scFv using E. coli but not the production of scFv using animal cells in serum-free medium. When E. coli is used as host cell, the produced protein is not secreted outside cells but remains in bacterial body, in what is called an inclusion body, which contains the protein in an inactive form. Therefore in order to obtain a protein in active form it is necessary to destroy the bacterial body and then to refold the product as described in Verma, page 167, right column, second paragraph. On the contrary the present invention produces the protein in an active form by using animal cells and serum-free medium, which is not obvious from Kortt using E. coli.

Dorai does not teach or suggest the use of serum-free medium by which an active dimer is formed. Therefore the present invention is not obvious from Dorai.

Keen discloses only whole antibodies (full length IgG) but not at all fragmented antibody molecules such as Fab, Fv, scFv or the like. When the structure of full length IgG is compared with that of scFv, it is apparent to a person skilled in the art that scFv lacks constant regions (CH and CL) and the lack may make hydrophobic amino acids, which are not exposed on the surface in the full length IgG, exposed on the surface which causes the

difference of stability. Furthermore Keen does not suggest the formation of an active dimer of scFv. Therefore it is not obvious to the person skilled in the art who has read Keen that an active dimer of scFv having a linker of 2-12 amino acids can be formed in serum-free medium.

Even if the cited references are combined, it would not have been obvious to a person of ordinary skill in the art that a dimer of scFv can be formed by using serum-free medium in an active form. The cited references do not teach or suggest all of the features of the claims and one of ordinary skill in the art would not have had a reasonable expectation of success of the present invention.

Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date July 31, 2006

By _____

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